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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,542	10/07/2004	Neil Lee Spector	PU4725USW	8482

23347 7590 04/23/2007

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,542	SPECTOR ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,18,25,29,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,18,25,29,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1, 3-5, 16-18, 25, 27 and 29, in the reply filed on 3/29/2007 is acknowledged.

Applicant's election without traverse of the compound of Formula III as recited in claim 5, in the reply filed on 3/29/2007 is acknowledged.

Status of the Claims

Claims 5, 18, 25, 29, 31 and 32 are currently pending and are the subject of this Office Action. Claims 1-4, 6-17, 19-24, 26-28 were cancelled in the amendment filed 3/29/2007. All pending claims read on the elected invention and are presently under examination.

Priority

This application is filed pursuant to 35 U.S.C. § 371 as a United States National Phase Application of International Application No. PCT/US03/10747 filed April 8, 2003, which claims priority from US 60/370,807 filed April 8, 2002.

Support for the instantly claimed invention was found in priority document 60/370,807 (*e.g.*, claims). As such, the earliest effective U.S. filing date afforded the instant claims has been determined to be April 8, 2002.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 10/7/2004. Examiner has considered the references cited therein to the extent that each is a proper citation. Please see attached USPTO Form 1449.

Drawings

The informal drawings are not of sufficient quality to permit examination. Accordingly, replacement drawing sheets in compliance with 37 CFR § 1.121(d) are required in reply to this Office action. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR § 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

Applicant is given a TWO MONTH time period to submit new drawings in compliance with 37 CFR § 1.81. Extensions of time may be obtained under the provisions of 37 CFR § 1.136(a). Failure to timely submit replacement drawing sheets will result in ABANDONMENT of the application.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 18, 25, 29 and 31-32 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the treatment of breast, head and neck, gastric, and pancreatic cancers, does not reasonably provide enablement for the treatment of all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404

[1] As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

wherein, citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) The breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to the general treatment of cancer comprising administering a compound of formula (III) as recited in instant claim 5 and a cRaf-1 or bRaf inhibitor. The invention thus entails a combination therapy for the general treatment of cancer. It is noted that

while the instant specification specifically describes two general classes of cRaf-1 and bRaf inhibitors, the instant claims encompass the administration of any compound that inhibits cRaf-1 and/or bRaf. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Gura *et al.* (Science, 1997, 278:1041-1042) and Johnson *et al.* (British J. of Cancer, 2001, 84(10):1424-1431).

Gura *et al.*, cited for evidentiary purposes, teaches that researchers face the problem of sifting through potential anticancer agents to find the ones promising enough to make human clinical trials worthwhile and further teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second paragraphs). It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. Also, with regard to unpredictability, Johnson *et al.*, also cited for evidentiary purposes, teach that the *in vivo* activity of 39 different agents in a particular histology in a tumor model did not correlate to activity in the same human cancer. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Further, the mode of action of anticancer agents is often unknown or very unpredictable and administration of such agents is often accompanied by undesirable side effects.

These articles plainly demonstrate that the art of treating cancer, particularly in humans, is extremely unpredictable, particularly in the case of a single compound or genus of compounds being used to treat any and all cancers.

2. The breadth of the claims

The claims are extremely broad insofar as they disclose the general treatment of cancer with the same combination of active agents. The claims are also broad insofar as they recite two genera of inhibitors (cRaf-1 and bRaf) with no limitation on structural features of said inhibitors or specific inhibitors.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to treat all cancers, particularly in humans. The disclosure recites extremely broad dosage ranges (*e.g.*, 0.1 to 100 mg/kg per day of the active agents (page 117, lines 23-25). Further, it is stated that the effective amounts will "depend on a number of factors" including the age and weight of the patient, the condition being treated, the severity of the condition, the nature of the formulation and the route of administration. No specific administration regimens are disclosed for the instantly claimed combination therapy. The working examples (with respect to cancer treatment) are limited to demonstrating the effects of combined therapy (with only two specific cRaf-1 and bRaf inhibitors) on the *in vitro* cell proliferation of pancreatic cancer cell lines. It is noted (see WO 99/35146) that the instantly claimed compound (GW572016; Lapatinib) has been shown to also be effective in inhibiting breast, head and neck, and gastric cancer cell growth *in vitro*.

Given the state of the prior art and the working examples of the present application, Applicants at best have provided specific direction or guidance only for the treatment of breast, head and neck, gastric, and pancreatic cancers with the instantly claimed drug combinations. No reasonably specific guidance is provided concerning useful therapeutic protocols for any other cancers and the skilled artisan would not have a reasonable expectation that the claimed combinations could predictably be used to treat any and all cancers.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed drug combination could be predictably used as a treatment for all cancers as inferred in the claims and contemplated by the specification. The art of treating cancer (especially in a human) is extremely unpredictable. It is noted that there is currently no drug or drug combination that is used clinically to treat cancers with different etiologies and treatment regimens. For example, although the anticancer drug paclitaxel has demonstrated efficacy in a wide range of cancers when tested *in vitro* and *in vivo*, it is generally not accepted that this drug can be used clinically to treat any and all cancers. As such, and in view of the above discussion, the skilled artisan would be faced with undue experimentation to determine exactly which combination of drugs and administration regimens are effective for any particular cancer. Further, although *in vitro* efficacy may be used to direct the course of experimentation, it is generally not accepted in the field of cancer therapy that *in vitro* (or even *in vivo*) data is generally predictive of efficacy in the clinic. Accordingly, the instant claims do not

comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 5, 18, 25, 29 and 31-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Carter *et al.* (WO 99/35146; Published July 15, 1999) (newly cited art).

Instant claim 5 recites a method of treating cancer comprising administering a compound of formula (III) and a cRaf-1 inhibitor. As noted *supra*, while the instant claims are not enabled for the general treatment of cancer, they are enabled for the treatment of breast, head and neck,

gastric, and pancreatic cancers. As such, the instant rejection is limited to the obviousness of treating breast, head and neck, gastric, and pancreatic cancers with the instantly claimed drug combination.

Carter *et al.* disclose methods of treating human malignancies, including breast, gastric, head and neck, and pancreatic tumors, especially those driven by EGF-R or erbB-2, comprising administering compounds of formula (I) (page 3, lines 4-12; page 3, line 24 to page 13, line 26; page 50, lines 10-17). Preferred compounds of the invention include the instantly claimed compound (page 37, lines 33-34 and page 100, Example 29). Salts of the compounds disclosed in Carter et al. are taught at page 40, lines 5-14 and reasonably suggest the instantly claimed monohydrate ditosylate salt of the compound of formula (III) as instantly claimed. Carter *et al.* suggest that the compounds of the invention "and their salts and solvates" may be employed alone or in combination with other therapeutic agents for the treatment of cancer (page 54, lines 8-10). For anticancer therapy, combination with other chemotherapeutic, hormonal or antibody agents is envisaged (*id.* at lines 10-11). The reference thus provides explicit motivation to combine the instantly claimed compound with other chemotherapeutic agents for the treatment of cancer. The instantly claimed compound of formula (III) was shown to effectively inhibit the growth of HB4a (erbB2) mammary cells, BT474 breast cancer cells, HN5 head and neck cancer cells and N87 gastric cancer cells (page 110, Table 2, Example 29). HB4a mammary cells transfected with H-ras cDNA were not inhibited by the claimed compound (*id.*).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed methods of treating cancer would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Carter *et al.* explicitly

suggests and provides the skilled artisan with the motivation to combine erbB2 inhibitors (such as a compound of formula (III)) other chemotherapeutic agents for the treatment of cancer. As such, it would have been obvious to one of ordinary skill in the art to combine a compound of formula (III) with other chemotherapeutic agents, including the instantly claimed cRaf-1 and bRaf inhibitors.

Claims 5, 25 and 31-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Carter *et al.* (WO 99/35146; Published July 15, 1999) (newly cited art) in view of Dickerson *et al.* (U.S. Patent No. 6,268,391; Issued July 31, 2001) (newly cited art).

Instant claim 5 recites a method of treating cancer comprising administering a compound of formula (III) and a cRaf-1 inhibitor. As noted *supra*, while the instant claims are not enabled for the general treatment of cancer, they are enabled for the treatment of breast, head and neck, gastric, and pancreatic cancers. As such, the instant rejection is limited to the obviousness of treating breast, head and neck, gastric, and pancreatic cancers with the instantly claimed drug combination.

Carter *et al.* disclose as discussed *supra*.

Dickerson *et al.* disclose compounds that can be used in the treatment of disorders mediated by cRaf1 kinase (Abstract). cRaf1 kinase is deregulated by events that are common in human cancer. For example, ras genes are mutated with the following frequencies in the following representative primary tumors: lung, 30%; colon, 50%; pancreatic, 90% (col. 2, lines 53-58). cRaf1 is also activated by deregulation of tyrosine kinases including, cSrc, ErbB2, EGFR and bcr/abl. These events are associated with breast, colon, and lung carcinomas (*id.* at lines 60-63). Dickerson *et al.* thus provide compounds (col. 4, line 1 to col. 23, line 47) for the

treatment of human malignancies, including breast, pancreatic and gastric cancer (col. 3, lines 35-47 and col. 23, lines 49-60). Combination therapy with other known anti-tumor therapies for more effective treatment of such tumors is disclosed (col. 24, lines 36-40). The reference thus provides the motivation to combine an inhibitor of cRaf1 with other anti-tumor agents for the treatment of cancer. The effectiveness of representative compounds of the invention in inhibiting colon, pancreatic, breast and prostate cancer cell growth is demonstrated in Table 4 (col. 102).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed methods of treating cancer would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. The instantly claimed compound of formula (III) and cRaf-1 inhibitors were both known in the art to inhibit the *in vitro* growth of the same cancer cell lines (*e.g.*, breast and pancreatic). Further, Carter *et al.* and Dickerson *et al.* both suggest and provide the skilled artisan with the motivation to combine erbB2 inhibitors (such as a compound of formula (III)) and cRaf-1 inhibitors for the treatment of cancer. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960).

Accordingly, to establish obviousness in such fact situations it is NOT necessary that the motivation come explicitly from the reference itself (although the Examiner believes it does, as discussed *supra*). The natural presumption that two individually known anticancer agents would,

when combined, provide a third composition also useful for treating cancer flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (*e.g.* unexpected results) to rebut this natural presumption.

Further, erbB2 inhibitors and cRaf-1 inhibitors have different mechanisms of action and cRaf-1 is activated by deregulation of tyrosine kinases including, cSrc, ErbB2, EGFR and bcr/abl (Dickerson *et al.* at col. 2, lines 60-63). As such, the skilled artisan would have been imbued with at least a reasonable expectation that a combination of a compound of formula (III) and a cRaf-1 inhibitor would be an effective treatment of breast, pancreatic, gastric or head and neck cancer.

Claims 18, 29 and 31-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Carter *et al.* (WO 99/35146; Published July 15, 1999) (newly cited art) in view of Dean *et al.* (WO 02/24680; Published March 28, 2002) (newly cited art).[2]

Instant claim 5 recites a method of treating cancer comprising administering a compound of formula (III) and a cRaf-1 inhibitor. As noted *supra*, while the instant claims are not enabled for the general treatment of cancer, they are enabled for the treatment of breast, head and neck, gastric, and pancreatic cancers. As such, the instant rejection is limited to the obviousness of treating breast, head and neck, gastric, and pancreatic cancers with the instantly claimed drug combination.

Carter *et al.* disclose as discussed *supra*.

[2] Dean *et al.* qualifies as prior art under 35 U.S.C. § 102(a) as it was published "by another" before the present invention.

Dean *et al.* disclose novel compounds and their use as Raf kinase inhibitors for the treatment of cancer (Abstract; page 11, lines 5-8). Inhibitors of Raf kinases have been suggested for use in the disruption of tumor cell growth and hence in the treatment of cancers, *e.g.*, histiocytic lymphoma, lung adenocarcinoma, small cell lung cancer and pancreatic and breast carcinoma (page 1, lines 17-19). The compounds disclosed in Dean *et al.* are inhibitors of Raf kinases, in particular inhibitors of B-Raf kinase (*id.* at lines 26-27).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed methods of treating cancer would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. The instantly claimed compound of formula (III) and bRaf inhibitors were both known in the art as treatments for cancer (*e.g.*, breast and pancreatic) via inhibition of erbB2 kinase and bRaf kinase. Further, Carter *et al.* provides the skilled artisan with the motivation to combine erbB2 inhibitors (such as a compound of formula (III)) and other chemotherapeutic agents for the treatment of cancer. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960).

Accordingly, to establish obviousness in such fact situations it is NOT necessary that the motivation come explicitly from the reference itself (although the Examiner believes it does, as discussed *supra*). The natural presumption that two individually known anticancer agents would, when combined, provide a third composition also useful for treating cancer flows logically from

each having been individually taught in the prior art. Applicant has presented no evidence (*e.g.* unexpected results) to rebut this natural presumption.

Further, erbB2 inhibitors and bRaf inhibitors have different mechanisms of action. As such, the skilled artisan would have been imbued with at least a reasonable expectation that a combination of a compound of formula (III) and a bRaf inhibitor would be an effective treatment of breast, pancreatic, gastric or head and neck cancer.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

U.S. Patent No. 6,727,256

Claims 5, 18, 25, 29 and 31-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-8 of U.S. Patent No. 6,727,256. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method claims of U.S. Patent 6,727,256 are drawn to the treatment of cancer comprising administering the instantly claimed compound and "pharmaceutically acceptable salts or solvates thereof" (see claim 5).

The "comprising" language of the '256 patent claims allows for the presence of other therapeutic agents, including the instantly claimed cRaf-1 and bRaf inhibitors.
See M.P.E.P. § 2111.03. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, *e.g.*, *Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended."). *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.)

As such, it would have been *prima facie* obvious to one of ordinary skill in the art to administer the compounds recited in the '256 patent claims in combination with other chemotherapeutic agents for the treatment of breast or head and neck cancers. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960). The natural presumption that two individually known anticancer agents would, when combined, provide a third composition also useful for treating cancer flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (*e.g.* unexpected results) to rebut this natural presumption.

For at least the reasons discussed *supra*, the instantly claimed methods are not patentably distinct from the methods claimed in U.S. Patent No. 6,727,256.

U.S. Patent No. 6,713,485

Claims 5, 18, 25, 29 and 31-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-6 of U.S. Patent No. 6,713,485. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method claims of U.S. Patent 6,713,485 are drawn to the treatment of breast, gastric or head and neck cancer comprising administering the instantly claimed compound or "pharmaceutically acceptable salts or solvates thereof" (see claim 5).

The "comprising" language of the '485 patent claims allows for the presence of other therapeutic agents, including the instantly claimed cRaf-1 and bRaf inhibitors. See M.P.E.P. § 2111.03. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, *e.g.*, *Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended."). *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.)

As such, it would have been *prima facie* obvious to one of ordinary skill in the art to administer the compounds recited in the '485 patent claims in combination with other chemotherapeutic agents for the treatment of breast or head and neck cancers. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960). The natural presumption that two individually known anticancer agents would, when combined, provide a third composition also useful for treating

cancer flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (*e.g.* unexpected results) to rebut this natural presumption.

For at least the reasons discussed *supra*, the instantly claimed methods are not patentably distinct from the methods claimed in U.S. Patent No. 6,713,485.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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April 16, 2007

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